REMARKS

Claims 1-17 were pending in the above-identified application prior to entry of this Amendment. After entry of this Amendment, claims 1-17 are pending in this case. Applicants note that in the Office Action dated November 11, 2004 the disposition of only claims 1-15 is indicated. It is respectfully requested the status of claims 16 and 17 be noted in future communications.

Rejection Under 35 U.S.C. §103(a)

The examiner has rejected claims 1-15 under 35 U.S.C. §103(a) as allegedly obvious in light of Kennedy (US 5,912,237), Feller et al. (US 4,816,446), Teng (US 4,510,135), Kennedy et al (US 3,330,327), Frederiksen (US 5,626,904), Huang et al. (CN 1,219,058 a), Martin et al. (Physical Pharmacy, Fourth Edition. Lea & Febiger 1993) and R. Simon (Dryers) Ltd. Website (www.simon-dryers.co.uk/drum/index.htm Copyright 1998-2003). This rejection is respectfully traversed.

To establish a prima facie case of obviousness, three basic criteria must be met.

(1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings.

(2) There must be a reasonable expectation of success.

(3) The prior art references must teach or suggest all the claim limitations. See *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2143 et seq. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. Id. The mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. See *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP §2143.01. A prior art reference must be considered in its entirety, including portions that lead away from the

claimed invention. See *W.L. Gore & Associates, Inc.v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983).

As stated in *In re Dow Chem. CO. v American Cyanamid Co.* U.S.P.Q. 2d 1529, 1532-32, "[t]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." Additionally, the Federal Circuit has stated that "[c]are must be taken to avoid hindsight reconstruction by using the patent in suit as a guide through the maze of prior art references, combining the right reference in the right way so as to achieve the result of the claims in suit" (see, *Grain Processing Corp. v American Maize-Prods. Co.*, U.S.P.Q. 2d 1788, 1792). It is respectfully put forth that the Examiner has used the Applicant's present disclosure, with the aid of hindsight, to reconstruct the claimed invention from a variety of isolated pieces of art in contravention of the statutory mandate of 35 U.S.C. §103(a) which requires judging obviousness at the point in time when the invention was made.

Although the examiner has stated that "Huang et al. provides the motivation to modify processes to produce a solid form of heparin because it is a goal of heparin manufacturing to increase production efficiency and to lower production costs by creating a continuous method of manufacturing (see abstract)," neither Huang nor the other references cited by the Examiner provide the motivation to combine them in order to arrive at a method for processing a solution containing a heat sensitive biologically active agent such as heparin in a solvent or a mixture of solvents to a dry solid form of heparin characterized by the use of a drum dryer at atmospheric pressure or under vacuum and at a suitable drying temperature.

The references cited by the Examiner also fail to disclose all of the claim limitations. For example, none of the references disclose the production of a solid form of heparin with the activities of at least 140 mg/mg.

One of skill in the art would not have been motivated to combine the teachings of the references cited by the Examiner to arrive at that the presently claimed invention. The R. Simon Dryers reference cited by the Examiner discloses the use of a drum dryer for drying starches. The reference however, only teaches about starches in general not the glycosoamino-glycans such as heparin whose utility resides in their biological activity which is sensitive to high temperatures. As stated in the specification on page 2, lines 9-

11, in order to preserve anticoagulant properties (potency), the process temperatures cannot exceed 100 °C reach for prolonged times especially during drying stages. The R. Simon Dryers reference would not motivate one of skill in the art to use a drum dryer to produce a solid form of a biologically active, heat sensitive, glycosoamino-glycan.

The Examiner has stated that Feller et al. discloses "alkali and alkaline earth metal salts can be made with natural heparin." There is no mention, teaching or suggestion however, that a solid form of heparin including an alkali metal or an alkaline earth metal salt of heparin, could be produced by the use of a drum dryer at atmospheric pressure or under vacuum and at a suitable drying temperature. There is also no mention, teaching or suggestion that a solid form of heparin could be produced at the activities disclosed in the present application (see Tables 1 and 2A where activities of drum dried purified and crude heparins are 175 u/mg and 162 u/mg, respectively). Feller only discloses an isolation process consisting of spray-drying or lyophilizing a heparin solution (col. 7, lines 1-2) to provide a white, amorphous, slightly hygroscopic powder (col. 7, lines 8-9) with an anticoagulant activity in the range of from about 1.0 to 20 IU/mg. Furthermore, there would be no expectation of success that a solid heparin possessing an activity of at least 140 mg/mg could be produced based on the teachings of Feller et al.

The Kennedy et al. reference is cited as teaching a method of drying aqueous solutions of heat sensitive compounds using drum dryers. The heat sensitive compounds disclosed in Kennedy et al. are detergent amine oxides. Such detergent compound are quite different from the presently claimed heparin. As the Kennedy et al. reference relates to the non-analogous art of detergent amine oxides, one of skill in the art would not have found it obvious to apply the teachings of the Kennedy et al. reference to produce a biologically active glycosoamino-glycan such as heparin whose biological activity is heat sensitive.

Furthermore, the Examiner's proposal for modifying the Kennedy reference in an effort to attain the claimed invention would destroy its intended function. As stated by the court in *In Re Fritch*, U.S.P.Q. 2d 1780, 1783, "[a] proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose." Kennedy is directed toward heparin for the inhibition of elastase and cathepsin. He specifically discloses the presence of

anticoagulant activity is something that is undesirable (see col. 3, lines 25-28). The present invention, in contrast, is directed toward a method of producing a solid form of heparin with high anticoagulant activity (see Tables 1, 2 and 2A, as well as page 4, lines 23-26).

In view of these remarks, withdrawal of the rejections under 35 U.S.C. §103(a) is respectfully requested.

It is respectfully submitted that the claims are in condition for allowance. Notification to this affect is earnestly solicited. The Examiner is encouraged to contact the Applicants' undersigned attorney to discuss this matter if any questions should arise upon further examination of the pending claims.

Respectfully submitted,

FEBRUARY 11, 2005
Date

Andrew J. Leon
Reg. No. 46,869